

## THE CONTROL OF CHOLERA \*

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WHEN, like the Huns of old, cholera swept from Asia into Europe, it wreaked havoc indeed. As it spread into Russia in 1830, 10% or more of the population of cities might die within a few weeks, often literally within hours after onset. Since it affected principally the poor and the destitute, many considered it a divine and just punishment. Unfortunately appropriate prayers to control the epidemic were not discovered. A more pragmatic Russian government established quarantines around infected communities, hoping by physical restraint to check the spread of the disease. Despite rigorous enforcement with floggings and executions, this measure also failed. A situation developed which was described by a contemporary Russian writer thus: "What is remarkable is the terror which the cholera inspires among people who count the plague as nothing. From the first noble to the last slave . . . all flee the sick and abandon them to their own devices. All natural bonds disappear, and as honor no longer exists, egoism appears in all its nakedness, in all its horror."<sup>1</sup> The military cordon failed before these pressures, and even the double cordon established around Vienna did not prevent the entry of cholera in 1831.

The medical profession was as confused by cholera as the lay public. Unlike smallpox, the chain of infection was not obvious, so that a great dispute ensued whether the disease was contagious or not. The resemblance of the cholera case to arsenic poisoning was recognized, and indeed rumors spread several times that this disease was in fact a mass poisoning of the common people by the nobility or, on occasion, by the medical profession. In the ensuing riots, the police and governmental officials were attacked. On at least one occasion, physicians were slaughtered, and the sick were removed from the cholera hospitals to save

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them from the black magic presumed to be practiced by the doctors.

It took the careful studies of John Snow in 1849 to 1855 to introduce the first pertinent glimmer of sense.<sup>2</sup> Logical analysis of carefully collected data on mortality led this anesthesiologist to the hypothesis that cholera evacuations were being mixed with water used for drinking and that this caused the disease. Snow tested his hypothesis by comparing the incidence of cholera in the customers of two different water companies. He was able to demonstrate that the mortality rates were 14 times higher among those using unfiltered Thames River water than among those whose water came from a better source. His dramatic removal of the handle of the Broad Street pump was a logical direct action. The subsequent absence of new cases is usually attributed to this act; the modern day epidemiologist is more impressed by the fortunate timing since the epidemic had already exhausted the supply of susceptibles.

Despite this understanding of the spread of disease, pandemics recurred again and again to run their natural course. In 1883 Robert Koch isolated the etiological organism and, within a year, J. Ferrán introduced immunization against cholera. Ferrán injected 1 ml. doses of living culture of the organisms; the severe reactions, sometimes including death, were felt justified in the face of so catastrophic a disease. Unfortunately adequate proof that it was protective could not be developed. Subsequent studies with different vaccines, including a living attenuated vaccine prepared by Waldemar M. Haffkine as well as killed vaccines, have indicated varying degrees of protectiveness. While some of the studies were well-designed, others had defects so that there was doubt whether the vaccine protected against cholera.<sup>8</sup>

International sanitary conferences in Constantinople in 1866 and in Vienna in 1874 established the concept of international quarantine and quarantine stations. The measures for international control of cholera in the 1960's were based on these facts and observations. A traveler who had been immunized within a six-month period could come from an infected area and move freely throughout the world, although surveillance might be maintained for five days. Improved sanitation was advocated; indeed cholera gave great impetus to the establishment of safe supplies of drinking water. In fact, the epidemic of 1832 is credited with being the force which established the Croton Aqueduct as the source of potable water for the City of New York; this source replaced

a supply used only by those who could not afford to have water brought into the city in hogsheads from "pure" springs and wells in the countryside.<sup>4</sup>

The studies carried out over the past 10 years have provided much information on which to develop a more logical set of control measures. For once, studies were under way before the epidemic hit, a circumstance for which credit must be given not to the foresight of a bacteriologist, but to that of an eminent authority in the field of rickettsiae and viruses, the late Joseph E. Smadel.

Properly designed and adequately controlled field studies have been carried out that have tested the efficacy of various cholera vaccines in Pakistan,<sup>5, 6</sup> India,<sup>7</sup> and the Philippines.<sup>8</sup> Whole cell vaccines and purified derivatives produced a significant reduction in the incidence of clinical disease, with 50 to 90% fewer cases than occurred in comparable groups who received a control vaccine (typhoid vaccine or tetanus toxoid). Unfortunately this protection lasted for only a short time, so that the vaccine must be given within a few months before exposure to disease is expected if it is to be protective. Further, difficulty is encountered in carrying out the immunization program. Those who volunteer for vaccination are usually the better-educated members of higher social levels who very rarely develop cholera. Those under the greatest risk of acquiring cholera are those who are most reluctant to accept the vaccine; great effort and expense is required to find and protect those who need it!

Field studies have clearly demonstrated that the classical dehydrated cholera patient represents the peak of the iceberg with many, many more asymptomatic cases or cases with simple diarrhea.<sup>9, 10</sup> The vaccine studies have shown that while vaccination does reduce the incidence of manifest disease, no clear reduction in the number of carriers can be assumed.<sup>5</sup> Clinical studies have shown that a carrier state can persist for prolonged periods of time,<sup>11</sup> and that this carrier state can persist as a biliary infection with negative stools and rectal swabs, so that infection can be demonstrated only by culturing duodenal aspirates or saline purge fluid.<sup>12</sup>

Failure of quarantine measures was predicted 100 years ago on the basis that those most likely to carry the organism would probably not be so considerate as to report to quarantine stations. Experience has borne this out in that many introductions of disease into clean areas

CONTROL OF CHOLERA IN THE 1970's

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- 1) Effective treatment of cholera as a diarrheal case.
  - 2) Bacteriological surveillance of diarrheal diseases.
  - 3) Chemoprophylaxis for members of the patient's hearth-group.
  - 4) Sanitary improvements:
    - Water supply.
    - Disposal of excreta.
  - 5) Health education.
  - 6) Immunizations on a voluntary basis.
  - 7) Elimination of quarantine measures.
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have been attributed to smugglers, fishermen, or others who cross borders at undesignated points. Among those who do properly pass through the quarantine station, vaccine will not assure that the traveler is not a carrier and it will not guarantee that the individual may not develop clinical disease. Even when excessive measures have been applied by some countries, a rectal swab and a requirement for a negative culture will not detect the individuals whose gall bladders and duodena contain cholera vibrios which, under appropriate conditions, can transit the intestinal tract.

What, then, is the appropriate control program for the 1970's? I give first priority to the implementation of the very effective treatment now available (see accompanying table). The treatment of cholera is that of any dehydrating diarrhea regardless of etiologic organism. The countries where cholera is most likely to occur are those in which diarrhea is a common disease; dehydrating diarrheas not associated with infection from *Vibrio cholerae* occur frequently. Intravenous rehydration fluid must be available without delay where and when the case may occur. This will be so only when cases of diarrheal disease are treated as though they had cholera; this will establish and maintain skill in the practitioners; it will also assure a flow of supplies for intravenous and oral therapy to the places of need. When the public knows how effective cholera treatment can be, panic is allayed, confidence is generated, and the cooperation of the population is insured. In his report to the Executive Board of WHO, Dr. Marcelino G. Candau, director-general, stated in January 1971 that "Today, cholera is one of the most rewarding diseases to treat; no patient with uncomplicated cholera arriving at the treatment center with his heart beating should

die. A moribund case of cholera given proper intravenous rehydration should be quite comfortable in a few hours time, and recovery is complete with no sequellae.”<sup>13</sup>

When cholera does enter a country the requirement for treatment materials and facilities will be sharply increased. This can be anticipated by early recognition that cholera vibrios are present in the population. This is best achieved by establishing adequate laboratory facilities for routine bacteriological surveillance of diarrhea cases. Only simple bacteriological techniques are involved. If the El Tor biotype is involved, culturing sewage may give early warning.<sup>14</sup>

When cholera is recognized in an individual, 10 to 20% of hearth-group contacts will be infected; some may develop disease while the others may spread the organisms.<sup>15</sup> The administration of 1 gm. of tetracycline daily for five days will free these individuals of infection, preventing secondary cases or spread of disease.<sup>16</sup>

The ultimate control of cholera rests in the development of a level of sanitation which will avoid fecal-oral transmission of the causal organism. Disease persists in areas of overcrowding and poor sanitation. The provision of a safe potable water supply and the establishment of techniques for safe excreta disposal provide better areas for investment of the time, effort, and money rather than dissipating these scarce resources in any immunization program. The part played by food,<sup>17</sup> whether contaminated by polluted water or by poor hygienic practices indicates the need for appropriate health education.

Immunization, shown to reduce significantly the risk to the individual, must be made available for those who desire it; but in the control of cholera in the community it plays a relatively minor role.

Many are now concerned about overpopulation and express concern that our preventive measures aggravate the problem. This is not a new concern; Bringham,<sup>18</sup> in 1832 published *A Treatise on Epidemic Cholera*, in which he states that in 1823:

In China, the ravages of the cholera were also great, in consequences of the numerous canals, and the immense population of the country. The Russian authorities urged the Mandarins to arrest the disease by adopting some preventive or preservative measures. But they were told in answer, that the malady would give more space in the world to those who survived it, and besides, that the cholera chose its victims from

among the filthy and the intemperate, and that no person of courage who lived with moderation and surrounded by cleanliness, would die of the disease.

We hope to achieve the cleanliness and must depend on family planning programs to provide the living space.

Here in the dispassionate atmosphere of a well-sanitated city which has had no case of cholera near it for more than 60 years we can draw up a modern control program, but outdated practices are still extant. Five years ago, a military cordon was established through the middle of Iran, preventing westward movement of anyone until chloramphenicol had been taken for three days. Within the year, a quarantine on travel was imposed in an area of a country where cholera appeared, resulting in dislocated persons with inadequate facilities. Some countries have denied the presence of the disease which was present, and others have imposed varying restrictive measures. To quote from the WHO Expert Committee on Cholera in 1967: "If, instead of taking excessive, ineffective and outdated measures, countries were to fight cholera in a spirit of international cooperation and in the light of modern scientific achievement, many lives and resources can be saved."<sup>19</sup> The United States has taken a positive lead in this direction by eliminating the requirement for cholera vaccination for travelers coming to this country from cholera-infected areas. In his statement, Dr. Jesse L. Steinfeld, Surgeon General of the U. S. Public Health Service, stated, "There is clear evidence that cholera vaccine is of little use in preventing the spread of cholera across borders. We have today excellent treatment for cholera; the only effective method for preventing the spread of disease is improvement of environmental sanitation."<sup>20</sup> The retention of the concept of quarantinability of this disease maintains the tendency to apply restrictive measures, even though they are admittedly ineffectual, and to foster nonreporting for fear that repressive measures will be applied against the reporting country with loss of trade or tourism.

In this country, if cholera should be imported, it would be no more than another case of diarrheal disease with strictly limited, if any, spread. With international cooperation and improvement of levels of sanitation and the standard of living, it is hoped that this will soon apply worldwide.

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